

UNIVERSITY OF TORONTO MEDICAL JOURNAL



OBSTETRICS AND GYNECOLOGY

Editorial		1
Welcome Freshmen!		1
Sterility in Marriage	J. Blumenstein, B.A., 5T8	3
Afibrinogenemia	N. Lloyd, B.A., M.A., 5T8	7
Diabetes Mellitus in Pregnancy	Margaret G. Norman, 5T8	10
"On Inspection"		12
Multiple Pregnancy	J. C. C. Alexander, 5T8	17
Vaginal Bleeding: Part I	P. G. Walfish, 5T8	21
Answers to "On Inspection"	B. M. Stewart, 5T8; R. C. Bull, 5T8	29
Book Reviews		30
News and Notes		31

NOVEMBER 1957

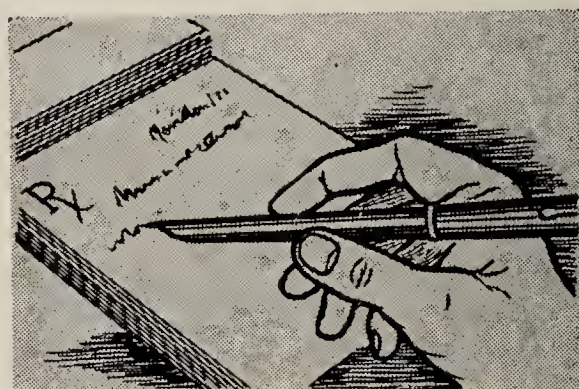
VOLUME XXXV

NUMBER 1

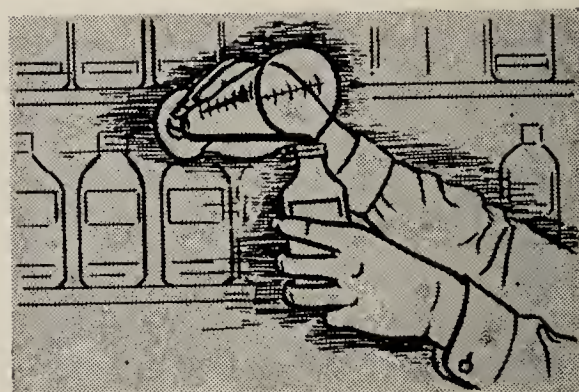
**more time
with your
family!**



► **when you
do this**



► **instead
of this**



Let the Pharmacist do ALL your dispensing

He is your full-time assistant, qualified to give you complete service in all things pharmaceutical.



THE ONTARIO RETAIL PHARMACISTS' ASSOCIATION

When your small patient requires vitamins A, D and C



prescribe

"OSTO A-D-C"

WATER-DISPERSIBLE to enhance absorption

MOST ECONOMICAL — precision dropper avoids waste

PLEASANT TASTING — children like it

Each 5-DROP DAILY DOSE

(0.25 cc.) contains:

Vitamin A (palmitate) 2000 Int. Units

Vitamin D 1000 Int. Units

Vitamin C 30 mg.

Available in bottles of 8, 15 and
30 cc., with calibrated dropper,
at a cost of 2½ to 3 cents per day.

Dose for dose, this "Frosst"
vitamin preparation costs
the patient less.

Charles E. Frosst & Co.
MONTREAL CANADA

CONCERTO WITHOUT COUGH

his physician prescribed

BENYLIN[®] EXPECTORANT

BENYLIN EXPECTORANT contains in each fluid-ounce:

Benadryl hydrochloride	80 mg.
(diphenhydramine hydrochloride, Parke-Davis)	
Ammonium chloride	12 gr.
Sodium citrate	5 gr.
Chloroform	2 gr.
Menthol	1/10 gr.

supplied: BENYLIN EXPECTORANT is available in 4-8 and 16-ounce and ½-gallon bottles.



PARKE, DAVIS & CO., LTD.
TORONTO 14, ONTARIO

UNIVERSITY OF TORONTO MEDICAL JOURNAL

ESTABLISHED DECEMBER 1923
AN UNDERGRADUATE PUBLICATION

VOLUME XXXV
NUMBER 1
TORONTO, NOVEMBER 1957



<i>Editor-in-Chief</i>	A. C. STRICKLER, 5T8
<i>Associate Editor</i>	P. C. F. MOORE, 5T9
<i>Assistant Editors: On Inspection</i>	R. C. BULL, 5T8
<i>Abstracts</i>	R. F. ARMSTRONG, 5T9
<i>Business Manager</i>	H. P. JAMES, 5T9
<i>Advertising Manager</i>	P. B. DENT, 6T0
<i>Premedical Representatives</i>	To be named

THIS JOURNAL is published six times a year from November to April, by the Medical Society of the University of Toronto, to serve primarily as a medium for student expression.

Subscription rates: \$3.50 for one volume of six consecutive issues. Single copies 65¢.

Manuscripts including references and footnotes should be typewritten double spaced on one side of the paper. References should be kept to a minimum, and should be cited numerically in the order in which they appear in the text.
Manuscripts in excess of 3,000 words will be considered *unsatisfactory*.
Illustrations are included by arrangement with the Editor. Drawings should be done on white paper in black ink.

Final copy date is the first day of *two months* prior to publication, e.g., September 1 for the November issue.

Material printed in this Journal is covered by copyright. Papers are accepted for consideration with the understanding that they are contributed for publication in this Journal only.
Correspondence should be addressed to Room 114, Medical Building, University of Toronto, Toronto 5, Ontario.

Authorized as Second Class Mail, Post Office Department, Ottawa.

EDITORIAL

THE 1957-1958 JOURNAL

Because of the overwhelming popularity of devoting monthly issues to individual specialties and body systems, this policy will be continued throughout Volume XXXV. Three of the topics to be used this year—Obstetrics and Gynecology, the Cardiovascular System, and Neurology and Psychiatry—have been considered in previous issues; however, since the scope of each of these subjects is almost limitless, it has been decided that further reference to them is in order. Two of the remaining issues will be concerned with Dermatology and Ophthalmology and Oto-laryngology. These topics have never been featured in this Journal. The final issue will consist of those papers whose subject matter does not conform to the main topics chosen for this year.

The feature "On Inspection" appears in this year's Journal for the first time. It is hoped that the use of photographs illustrating interesting conditions and problems in diagnosis will provide some variety and interest.

New books will be reviewed as they are received.

An attempt will be made to secure for publication the lectures delivered by visiting dignitaries. The value of having these lectures in a form in which later reference can be made to them is undisputed. Such lectures are of further interest in that they represent the work of medical contemporaries of international reputation.

Papers presented at Alpha Omega Alpha Honour Medical Society and Arts and Letters Club meetings will be published whenever possible.

A. C. S.

WELCOME FRESHMEN!

Welcome and Congratulations on entering *the* profession in Canada's foremost medical school. This thought should be digested in order to build an invincible confidence. You are embarking upon "the best work of all", and this will provide more incentive than any challenge thus far. And remember, security is not to be found by eliminating the challenge, but only in an inner assurance which no challenge can disturb.

And this assurance comes with being a bona fide member of the Faculty of Medicine, University of Toronto, and you in the first premedical and first medical years are just as important as any senior student—remember that. So govern yourself accordingly. You are a campus leader by heredity. Enjoy yourself in the best six years of your life, and may God's blessing be with you throughout the length of your journey.

CHUCK BULL
President, Medical Society

STERILITY in the family has long been attributed to the female. However, investigations in the last few decades have partly transferred the onus, and it is now believed that the male is responsible in at least one-third of the cases. The investigation and therapy of infertility is relegated to the gynecologist, or the urologist if the male is involved.

This paper will cover briefly the etiology, investigation and treatment of barren marriages.

DEFINITIONS

Many of the terms employed in connection with infertility are used differently by various authors. The following terms are generally accepted and are clear cut. Barrenness, infertility and sterility are interchangeable in all literature. *Primary* sterility occurs when conception has not resulted within one year of normal marital relations without the use of contraceptive measures. *Secondary* sterility is involuntary barrenness for one year following one or more successful pregnancies. *Relative* sterility is referred to when conception takes place with ease, but the female is unable to bear live offspring. This latter condition will not be discussed because it involves the very broad subject of habitual abortion. A *subfertile* individual is one who can reproduce only under ideal conditions.

INCIDENCE

The extensive use of contraceptives in North America prevents a reliable estimation of sterility from vital statistics. The incidence is variously estimated from a maximum of 13–17% (1928)¹ to a minimum of 10% (1956).² This produces a startling and alarming revelation: that

in the U.S.A. alone two million marriages are barren with the loss of a potential six million children.³

ETIOLOGY

According to Meaker,⁴ the human is a very poor breeder, and couples who reproduce do so against overwhelming odds. The following conditions have to be met for the reproductive process to function normally:

- a. the testes must produce a sufficient number of normal spermatozoa.
- b. the male genital tract must be patent to allow the spermatozoa passage.
- c. the prostato-vesicular secretion must be favourable to the spermatozoa.
- d. the ejaculated spermatozoa must be delivered near the external os of the cervix.
- e. the endocervical secretion must be favourable to the spermatozoa.
- f. the cervix and Fallopian tubes must be patent to allow for the passage of the spermatozoa.
- g. the ovaries must produce normal ova.
- h. the endometrium must be prepared to receive the fertilized ovum, and the corpus luteum must be maintained until the development of the placenta.

With these basic requirements in mind the causative factors of sterility may be divided into two groups: general and local.

In the group of **general** factors, similar conditions affect both sexes. Advanced reproductive age and barren marriages of long duration decrease the success of therapy. The *constitutional* abnormalities include systemic and chronic focal infections in places other than the genital organs as well as metabolic diseases. These have the effect of

either suppressing the development or of producing abnormalities in the germ cells in either sex. Among the *endocrine* dysfunctions, pituitary deficiency produces sterility even in the well developed male and sterility, obesity and amenorrhea in the female (adiposogenital dys trophy). Primary ovarian dysfunction as is associated with radiation therapy leads to infertility and amenorrhea. Anovulatory menstruation occurs frequently in some patients, and may be caused by a lack of luteinizing hormone, a lack of response of maturing follicle, or a thick fibrous capsule formed around the follicle produced by previous pelvic inflammation.⁵ Both hypo and hyperthyroidism may produce sterility in either partner, and the middle-aged obesity in the male sometimes associated with infertility may be traced to pituitary-thyroid imbalance. *Psychological* factors may also play a role. Mental overwork in the male often produces seminal deficiency. Impotency and loss of sexual desire are usually of psychic origin, but may also be attributed to local factors. In the female, dyspareunia and vaginismus, also factors in sterility, may be the result of abnormal mental attitudes.

Primary among the *local* factors affecting male sterility are the *congenital* abnormalities of the sex organs. These conditions may prevent normal delivery of the semen as in hypospadias or produce oligozoospermia as in undescended testes. *Inflammatory* occlusions of the genital tract caused by gonorrhea and less frequently tuberculosis also prevent the movement of the spermatozoa. Alteration in the composition of the prostatic-vesicular fluid due to chronic prostatic infection renders the spermatozoa ineffective.

Congenital abnormalities account for some cases of sterility in the female. These include congenital absence of the

uterus and imperforate hymen. Gonococcal and tuberculous *infections* result in obstruction of the Fallopian tubes. Nonspecific infections of the cervix and vagina may act in producing secretions hostile to the spermatozoa. Local inflammations of the vagina, Bartholin's glands, anal fissures and hemorrhoids may produce vaginismus, thereby interfering with the effective sex life of the female.

No attempt has been made here to list all the etiological factors, but a general outline is given. A single factor will not necessarily produce absolute sterility in the patient, but will render him or her subfertile. It is probable that more than one factor operates to render a person infertile. This is the principle of multiple causation proposed by Meaker⁶ who demonstrated that in 75 cases of female sterility, there were 165 local causative factors.⁴

INVESTIGATION AND TREATMENT

It is apparent that the causative factors of sterility are many, often complex and even multiple. The following is an outline for the investigation and treatment of barren marriages.

Holtz⁷ claims that following the investigation and treatment of each causative factor, a trial of reproduction should be attempted, with the patients returning to the doctor in six months if conception has not occurred. If the etiological factors are not investigated at the beginning of treatment, the time elapsed will add to the age of the patient and may preclude successful treatment. All factors must first be investigated since treatment of a single factor may neglect others operating in the same person.

The investigation begins with a complete history of both partners including a functional enquiry of all systems. Special emphasis on gynecological

history should take into account length of sterility, previous investigation and treatment, complete menstrual history, pelvic operations and childhood diseases. Length of marriage, history of contraception, previous marriages, pregnancies and abortions are all significant. The male should be asked, in addition to the functional enquiry, work habits, sexual desires and potency. A history of venereal infection is obviously important.

Both partners should undergo routine physical examinations. Gynecological examination should include a bimanual pelvic examination. Routine laboratory tests should be done at this time. If there is any evidence on physical examination of thyroid malfunction, a PBI is essential. Other more complex endocrine studies may be deferred until later. Gross pelvic abnormalities, foci of infection or other pathological conditions in either patient should be treated before investigation is resumed. If uterine fibroids are palpated, their examination with uterosalpingography is essential, and if they are cornual or submucous in location, myomectomy should be considered. Abnormalities in menstruation must be investigated and treated.

The next diagnostic test is a semen examination. The specimen is obtained in a clean wide-mouthed test tube following coital abstinence for at least two days. The semen is examined within two hours as to volume, pH, total spermatozoa per cc. and number of non-motile and abnormal forms in the specimen. The normal values are: volume 3-4.5 cc., pH 7.5, total number above 60,000,000 per cc., two hours after collection 65% of the spermatozoa should exhibit migratory movement, and not more than 15% should be abnormal. In the case of oligospermia or azospermia, 17-ketosteroid excretion is measured to indicate primary or secondary hypo-

gonadism, and a PBI reflects thyroid over- or under-activity. An investigation should be made as to whether the patient utilizes vitamins A, B, C and E from food. Exposure to radiation, high temperatures (steam baths) or too frequent coitus may also result in decreasing the sperm count.

In some cases of azospermia, where there is no apparent causative agent, there should be recourse to testicular biopsy. This may be done in the office under local anaesthesia by incising the skin of the scrotum and nicking the capsule of the testes. Pressure will express small amounts of testicular tissue which can be processed and examined histologically. Hormones may be used where faulty spermatogenesis is due to endocrine imbalance only. This can be assessed from the 17-ketosteroid excretion and the biopsy. The most successful treatment has been a combination of 1.0 mgm. of chorionic gonadotrophin with 2.5 mgm. of serum gonadotrophin. Intramuscular injections should be given daily for at least two months. Testosterone in high doses produces a "rebound" of spermatogenesis in 18% of patients who exhibited oligospermia, but its use is still limited. If testicular biopsy reveals degenerative changes and the etiological factors cannot be corrected, artificial insemination should be considered, *but carefully*.

If no cause for sterility can be found using the preceding methods, the Huhner test⁵ should be employed. This is a postcoital examination of the cervical secretions in the posterior vaginal fornix and the cervical canal. The test is performed 2-3 hours after non-prescribed coitus at the time of ovulation and preceded by a few days of sexual abstinence. The secretions aspirated separately from the posterior fornix and the cervical canal are examined under the high power of the

microscope. Absence of spermatozoa from the former area points to faulty delivery of the semen. Congenital abnormalities, impotence, vaginismus and faulty position during intercourse should be re-examined and corrected. Thirty actively migrating spermatozoa in the sample from the cervical canal is normal. A decrease in this number indicates hostility of endocervical secretions to the spermatozoa if a sufficient number were present in the posterior fornix. Pre-coital alkaline douche, Ringer-glucose pre-coital douche and estrogen therapy enhance the entrance and survival of the spermatozoa in the cervical canal.

When the Huhner test shows an adequate invasion of the cervical canal, tubal patency tests are performed. Two methods are used: trans-uterine insufflation by carbon dioxide (Rubin test) and uterosalpingography for the radiological observation of the passage of radio-opaque material through the Fallopian tubes. This method is also used to locate the site of tubal obstruction preparatory to operation. The Rubin test demonstrates tubal patency by passage of carbon dioxide at a regular rate under measured pressure into the uterus. An abnormal increase of pressure indicates tubal narrowing or occlusion. Correction of tubal stenosis is attempted by repeated trans-uterine insufflation under a pressure of 200–240 mm. of mercury, estrogen therapy (2 mgm. intramuscularly every fifth day $\times$ 5), trans-uterine injection of lipiodol under a pressure of 240 mm. of mercury and plastic surgery although the success of surgery is questionable.

An imbalance between estrogen and progesterone may produce a wide variety of conditions from anovulatory menstruation to inadequate preparation of the endometrium. The diagnosis of anovulatory endometrium is made by finding non-secretory endometrium prior to the onset of menstruation. Diagnostic curettage is the method of choice for obtaining the biopsy. Constant waking temperature during the menstrual cycle also points to anovulatory menstruation. This may be treated by 2.5 mgm. of serum gonadotrophin daily for the first six days of the menstrual period. Estrogen and thyroid therapy have also been employed. The lack of progesterone in the postovulatory phase of menstruation shows up in the endometrial biopsy as a glycopenia, and may deter implantation. The injection of 50 mgm. of progesterone every other day from the 12th to the 24th day of the menstrual cycle prepares the endometrium sufficiently.

When the conscientious physician has exhausted all available methods of investigation and treatment relating to a barren marriage, he should suggest that adoption be considered.

REFERENCES

1. LOTKA, A.: *Proc. Nat. Acad. Sc.*, 14: 99, 1928.
2. NOVAK, E. & NOVAK, E. R.: *Textbook of Gynecology*, 5th edition, 1956.
3. MEAKER, S. R.: *Human Sterility*, 1934.
4. DAVIS, C. H.: *Gynecology & Obstetrics*, Chapter 9, 1935.
5. MAZER, C., & ISRAEL, S. L.: *Menstrual Disorders & Sterility*, 3rd edition, 1951.
6. MEAKER, S. R.: *Practitioner*, 132: 326, 1934.
7. HOLTZ, D. F.: *Acta. Obstet. & Gynecol. Scand.*, 30: 259, 1950, Suppl. 7.

INTRODUCTION

SULFONAMIDES and antibiotics have reduced maternal mortality due to puerperal sepsis thus moving toxemia and hemorrhage into first place. This paper will concern itself primarily with one aspect of the hemorrhagic states of pregnancy, viz. hypofibrinogenemia. The obstetrical circumstances with which this condition is commonly associated are:

1. Abruptio placenta.
2. Amniotic fluid infusion (or embolism).
3. Missed abortion.

Also implicated are eclampsia and postpartum hemorrhage. Other conditions probably associated with defibrination are bilateral renal cortical necrosis, pituitary necrosis, traumatic forceps delivery, hydatidiform mole, and incompatible blood transfusions.

The most significant hematologic change which occurs in these patients is a defibrination of the blood.

Historically, De Lee in 1901 described severe, uncontrollable hemorrhage associated with failure of the blood to clot as a temporary state of hemophilia. In 1936 Dieckmann observed a decreased level of fibrinogen in patients who had hemorrhage following abruptio placenta. Recently many opinions concerning the theory of the physiologic and pathologic processes causing hypofibrinogenemia have been promulgated. An attempt will now be made to present some of these views.

DEFINITIONS AND MECHANISM

Afibrinogenemia and hypofibrinogenemia (fibrinogenopenia) refer to the respective conditions in which no fibrinogen is detectable in the circulating

blood and in which the concentration of fibrinogen is 100 mgm. or less per 100 cc. of plasma. These terms will largely be used interchangeably.

The normal levels of fibrinogen in gravidas at term range between 300 and 700 mgm. % (440 mgm. % is a good average figure). When the fibrinogen level falls below 100 mgm. %, the blood is deprived of its coagulative ability.

Although the clinical pictures will be considered separately in a subsequent section, it is well now to outline the fundamental underlying mechanisms which account for the hemorrhagic diathesis. This failure of coagulation has several possible explanations:

1. Immobilization of fibrin by thromboplastic substances released in the blood stream with resultant widespread intravascular clotting and consequent defibrination of the blood. These substances could enter the circulation by amniotic fluid infusion or embolism. Experimentally it has been demonstrated that thromboplastin infused intravenously will decrease the fibrinogen level. It is known that placental extracts and amniotic fluid possess thromboplastic activity.

2. Destruction of fibrin by fibrinolysin which is normally carried in the globulin portion of the blood. This mechanism is probably the exception rather than the rule.

3. Loss of fibrinogen through hemorrhage or excessive utilization at the site of placental separation.

4. It is also possible that the solubility of fibrinogen may be altered.

CLINICAL ASPECTS

1. ABRUPTIO PLACENTA

The premature separation of a norm-

ally implanted placenta is the most frequent cause of excessive blood loss in pregnancy, and hypofibrinogenemia is seen most commonly in association with severe cases of this condition, viz. 5–10% of abruptio placenta.

The pathogenesis of hypofibrinogenemia in relation to abruptio placenta is really a matter of conjecture. Dieckmann believes that the fibrinogen is lost through hemorrhage and utilization at the site of placental separation. Maloney *et al.* believe that the fibrinogen is destroyed by plasmin (the fibrinolytic enzyme of plasma that is active at the pH of blood). A more probable explanation, however, is that it results from intravascular coagulation of the maternal blood due to thromboplastic material gaining access to the maternal circulation.

As previously noted, the placental tissue is highly thromboplastic, and defibrination can be produced in experimental animals by the intravenous injection of placental tissue. It is indeed tempting to accept the explanation that the hypofibrinogenemia seen in abruptio placenta is due to the thromboplastic effects of placental tissue. This view is further supported by the autopsy finding in such patients of intravascular fibrin deposits throughout the body, particularly in the lungs, kidneys and liver. The excessive fibrinolytic activity may be accounted for by the concomitant shock, perhaps combined with normal increase in plasma fibrinolytic activity associated with parturition. The low concentration of the substrate fibrinogen would tend to further exaggerate the effects of any increased fibrinolytic activity.

Although the view that the decrease in fibrinogen is the result of intravascular defibrination is attractive, it is merely conjecture. It is possible, for example, that the solubility of the fibrinogen is reduced, and that this protein is then

precipitated in the small blood vessels as an insoluble substance that is not, however, true fibrin. Recent experimental data by Thomas suggest this latter possibility.

2. AMNIOTIC FLUID EMBOLISM

The patient with amniotic fluid embolus experiences vaginal bleeding not only because of possible hypofibrinogenemia, but also because she is in shock with consequent diminution of contraction of the myometrium.

Studies of amniotic fluid have shown that it contains thromboplastin in varying amounts, but it does not contain fibrinolysin. Ruptured membranes and a difficult labour could force amniotic fluid between the membranes and the wall of the uterus into the maternal sinusoids at the utero-placental site. Crossing the decidua this fluid acquires a high concentration of thromboplastin, thus producing an intravascular coagulation reaction, amniotic fluid embolus with anaphylactoid shock, and probably a total defibrination.

Autopsy reveals embolization of the maternal circulation by amniotic fluid; lanugo hairs and desquamated fetal epithelium (squames) are found in the mother's pulmonary vessels.

It seems tenable to accept the view that the coagulative defect with amniotic fluid embolus is due to the thromboplastic action of the infused amniotic fluid on the maternal blood.

Excessive plasma fibrinolysis has been reported, but this is not invariably present, and amniotic fluid itself is not fibrinolytic. As in cases of abruptio placenta, it appears reasonable to relate the excessive plasma fibrinolytic activity to the concomitant shock, combined with the postpartum state.

3. MISSED ABORTION

The occurrence of hypofibrinogenemia

in the face of retention of products of conception after fetal death has two prerequisites: first, that the pregnancy should have existed at least four months, and second, that the fetus be retained in the uterus for at least five weeks after death. Hypofibrinogenemia has not been reported in cases in which fetal death occurred earlier than the fourth month of gestation, nor has it been noted in less than five weeks after the apparent death of the fetus.

There has been no demonstration of significantly abnormal fibrinolytic activity in the blood of patients with hypofibrinogenemia associated with a retained dead fetus. Weiner *et al.* believe that the fibrinogen is consumed by intravascular coagulation, perhaps as a result of thromboplastic material from the dead fetus, from the placenta, or from amniotic fluid gaining entrance to the maternal circulation.

CLINICAL SUMMARY

Normal pregnancy is associated with an increase in fibrinogen in the maternal plasma, and during delivery there is normally an increase in plasma fibrinolytic activity which persists for several hours postpartum.

In some cases of abruptio placenta and amniotic fluid embolism, hypofibrinogenemia may develop acutely, and may be associated with uterine and generalized bleeding. It is postulated that thromboplastic tissue from the placenta in premature separation and from amniotic fluid in amniotic fluid embolism enters the maternal circulation, and causes intravascular coagulation with subsequent defibrination. In the case of intrauterine retention of a dead fetus where fetal death occurs in the fourth month of gestation or later, hypofibrinogenemia appears five or more weeks thereafter. In some cases the hypofibrinogenemia develops gradually and in

others, excessive bleeding at delivery is the first evidence of the condition. The mechanism responsible for the hypofibrinogenemia is unknown.

LABORATORY DETERMINATION

Hypofibrinogenemia or afibrinogenemia can be detected by observation of the effect of bovine thrombin on the patient's blood or by the actual determination of the concentration of fibrinogen in the patient's plasma. The accurate and full determination of the fibrinogen level is a laboratory procedure requiring at least one hour, which is too long a time in an obstetrical crisis.

In the simplified procedure, if the patient's blood, added to a tube containing thrombin, fails to form a clot, such a result is indicative of afibrinogenemia. If hypofibrinogenemia is present, a clot may form, but it is either small or shrivels after a few minutes. A firm clot that is of good size suggests that the blood contains a normal amount of fibrinogen. It is to be further noted that a sensitive indicator of hypofibrinogenemia is the separation of red blood cells from the clot as shown by Weiner *et al.*

In summary, when the blood is added to bovine thrombin, the normal patient will clot initially and the clot will remain intact, whereas the patient with hypofibrinogenemia forms a loose clot which contracts in a few minutes extruding all the red blood cells, and in afibrinogenemia no clot forms at all.

TREATMENT

From the point of view of therapy, the difference between hypofibrinogenemia and fibrinolysis is at present unimportant. The therapeutic principles of importance remain the same: prevention, accuracy of diagnosis, and adequacy of fibrinogen replacement.

1. ABRUPTIO PLACENTA

The treatment of a patient with a

hemorrhagic diathesis associated with premature separation of the placenta consists of three parts: first, treat for blood loss and shock as with any other patient; second, she should be given an intravenous injection of 4 Gm. of purified human fibrinogen; and third, measures should be taken to empty the uterus.

2. AMNIOTIC FLUID EMBOLISM

Treat for shock in the usual manner, and give 4 Gm. of fibrinogen intravenously.

3. MISSED ABORTION

Preventive therapy is the best approach in this particular problem. For cases in which death of the fetus is diagnosed, and in which the pregnancy is four months or more, intervention before the fifth week would avoid the threat of a declining fibrinogen level.

CONCLUSION

No final answer is as yet available to

account for the physiologic and pathologic processes of hypofibrinogenemia. With further understanding of the mechanisms involved, new therapeutic tools will become available.

BIBLIOGRAPHY

1. BARNES, A. C.: *Ann. Rev. Med.*, 7: 89-95, 1956.
2. DIECKMANN, W. J.: *Obs. et Gyn.*, 4: 159, 1954.
3. EASTMAN, N. J.: *Williams Obstetrics*, 1956.
4. HODGKINSON *et al.*: *Jour. Am. Med. Assoc.*, 154: 557, 1954.
5. MALONEY, W. C., *et al.*: *New Eng. Jour. Med.*, 240: 596, 1949.
6. MURPHY, C. J., *et al.*: *Am. Jour. Obs. et Gyn.*, 72: 1197, 1956.
7. PAGE, E. W.: *Obs., Gyn., et Surg.*, 3: 746, 1948.
8. RATNOFF, O. D., PRITCHARD, J. A., ET TOLOPY, J. E.: *New Eng. Jour. Med.*, 253: 63, 97, 1955.
9. THOMAS, L., *et al.*: *Proc. Soc. Biol. et Med.*, 86: 813-18, 1954.
10. WEINER, *et al.*: *Am. Jour. Obs. et Gyn.*, 66: 500-506, 1953.

DIABETES MELLITUS IN PREGNANCY*

MARGARET G. NORMAN, 5T8

CO-EXISTING pregnancy and diabetes was virtually unknown until the use of insulin in 1922. Up until 1909 only some 65 cases were reported in the literature. When it did occur, the prognosis was poor. The immediate maternal mortality was 25%, another 25% died within two years, and the foetal mortality was 50-75%.

In the last twenty years this picture has changed greatly. The incidence of diabetic pregnancy is about 1:500. Treated diabetics are not sterile, and the type of patient seen now is much

different. Prior to the use of insulin, women having diabetes were usually maturity-onset who did not have the extensive vascular damage seen in the juvenile diabetic who now survives to have children. The last change in this picture is the drop in maternal mortality to nearly zero. Maternal mortality is now due to obstetric rather than diabetic causes. The foetal mortality has dropped far more slowly, and now at best is 10%. It is the attempt to decrease foetal mortality which is receiving most attention now.

Untreated diabetics are almost invariably sterile, but sterility is rare in treated diabetics. This is partially due

*From an AOA paper by G. D. Blenkarn, M. M. Paul, and M. G. Norman.

to reversal of starvation by insulin, but it is also postulated that insulin reverses an "endocrine dysfunction" leading to sterility, the nature of this dysfunction being unknown.

The complications seen in a diabetic pregnancy increase with the severity of the diabetes; hence, classification as to degree of severity is of more than academic importance. Priscilla White's classification based on duration, age of onset of the diabetes, and degree of vascular damage is consistent with the great emphasis she places on vascular damage as one of the great dangers and complicating factors in diabetic pregnancy. The classification is as follows:

Class A: Glucose tolerance test diabetic, but no insulin required.

Class B: Age of onset 20 years, duration less than 10 years.

Class C: Age of onset 10-19 years, duration 10-19 years.

Class D: Age of onset under 10 years, duration more than 20 years, retinitis, and ankle vessel calcification.

Class E: Calcified pelvic vessels.

Class F: Diabetic vascular nephritis.

Classes A to E have to do with foetal risk, class F with maternal risk. Peder sen confirms this in a general way in that classes D to F have a higher foetal mortality than do classes A to C. White and Peel do not feel that the requirements of insulin or lability of the carbohydrate metabolism are factors in assessing the severity of the diabetes. Jones, however, finds that those patients requiring more than 50 units of insulin daily show a greater tendency to acidosis, and since acidosis is usually lethal to the foetus, he feels that insulin requirements should be given weight in classification along with the degree of vascular damage.

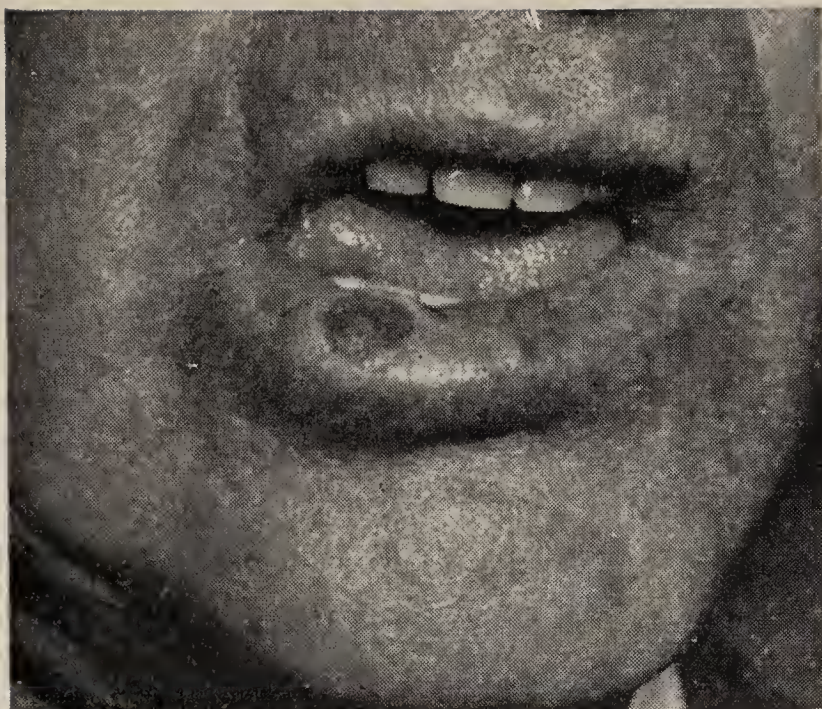
Another complication of the diabetes is derangement of carbohydrate metabolism. Most pregnant women show

decreased tolerance to carbohydrate and a decrease in fixed alkali. These tendencies are aggravated in diabetics, and are manifested by the great rapidity with which a diabetic pregnant woman can go into acidotic coma. This is only one of the reflections of the greater "lability" or "brittleness" of diabetes in pregnant women. The insulin requirements, however, are unpredictable, and may increase or decrease during pregnancy. The pregnancy does not make the diabetes worse. In fact, sometimes the insulin requirements are less after pregnancy than they were before pregnancy.

Although the pregnancy does not permanently affect the diabetes and metabolic state, it may make the vascular damage which comes prematurely to all diabetics worse. Increasing retinitis, retinitis proliferans, or signs of diabetic vascular nephritis can all begin during pregnancy.

Pregnancy complications seen more frequently are spontaneous abortion, toxemia, hydramnios and spontaneous onset of premature labour. Since the use of insulin abortion has decreased sharply from 30% to 15%, and some series report an incidence of spontaneous abortion not significantly different from that seen in the non-diabetic population.

Toxemia and hydramnios are both seen in increased frequency in diabetic pregnancies; however, since they occur in non-diabetic pregnancies, they cannot be attributed to the diabetes alone. Hydramnios differs in diabetic pregnancies in that it is usually not associated with congenital defects as it very often is in non-diabetic pregnancies. The reason for the increased incidence of toxemia in diabetic pregnancies is obscure. The incidence varies from 56% to 3%. It may be related to the vascular damage in diabetics, but there is no proof of this. It may also be related to



← FIGURE 1. No history needed here! What is your diagnosis? What is this man's likely environment? In what age-group is he? How would you treat him?

Careful observation often makes a diagnosis without the physician laying a hand or an instrument upon his patient. Here are six photographs to test your powers of observation. Each has enough clues for you to make the diagnosis.

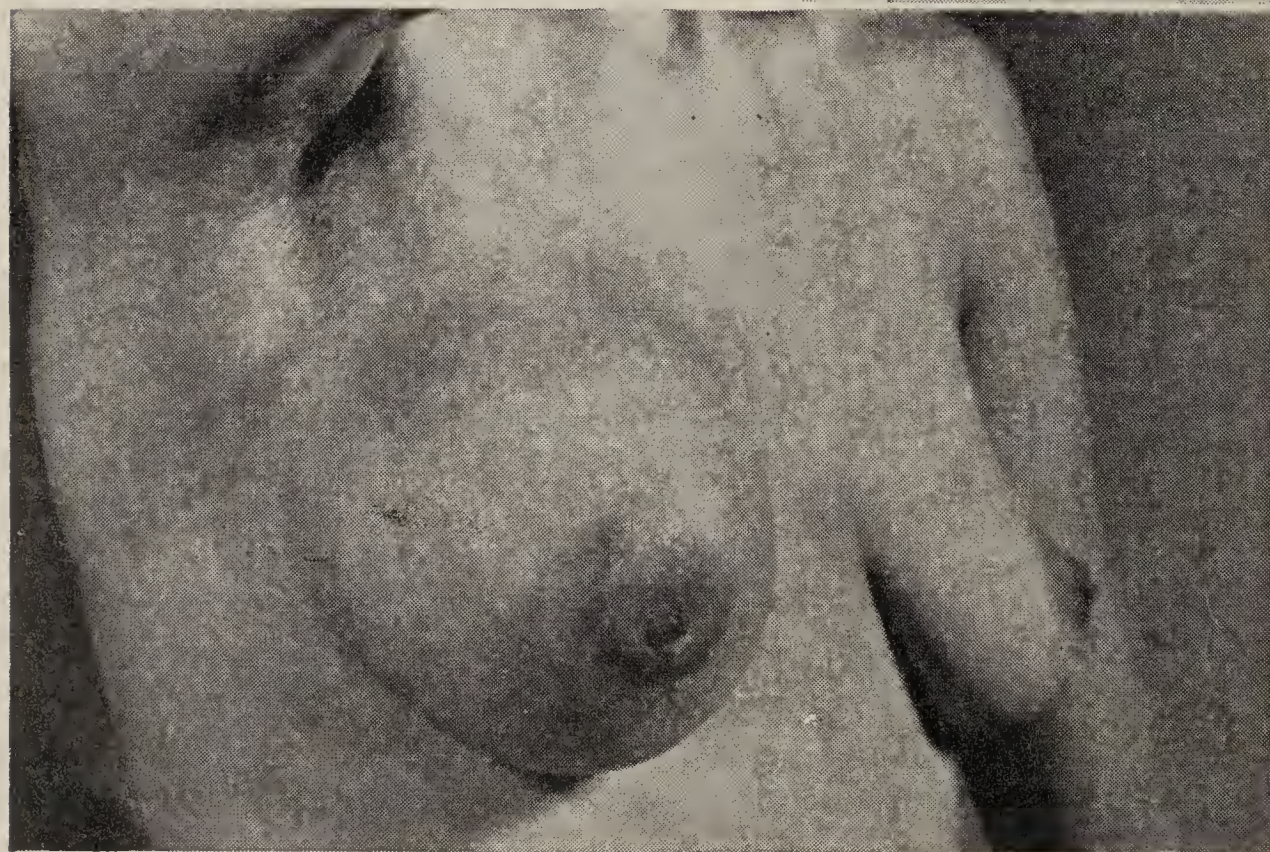
You will find the answers on page 29.



←

FIGURE 2. This 24-year-old European immigrant, presented with fever, anorexia, malaise and severe sore throat of three weeks' duration. On examination she was found to have these marks on her back.

What are these lesions? Describe their pathology.



↑ FIGURE 3. What is the differential diagnosis? What is your provisional diagnosis in this case?

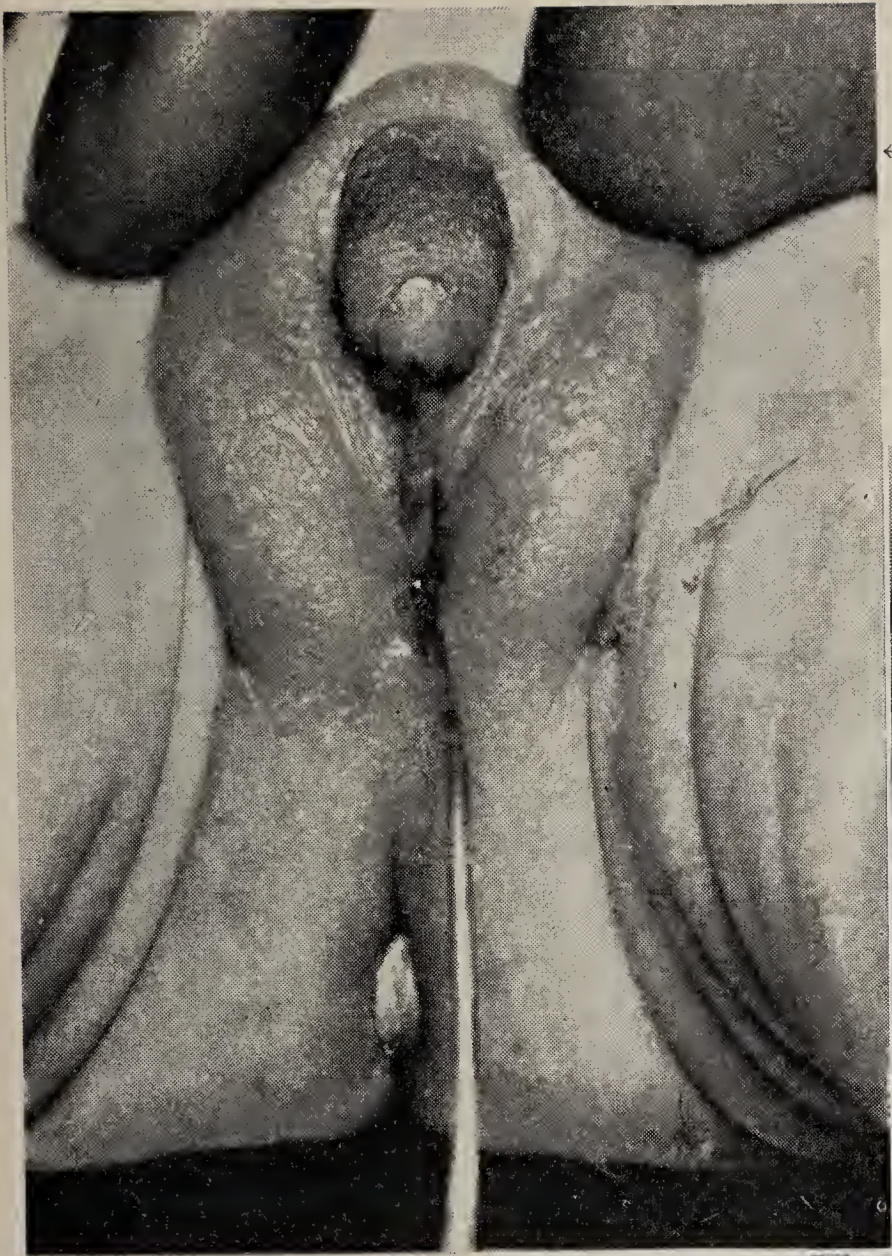


FIGURE 4. Careful scrutiny of this photograph will lead to a full diagnosis. What is the essential pathology? How would you treat him (or her)?

FIGURE 5. Describe the lesions visualized. What were the likely symptoms which brought this patient to hospital, and what was their likely etiology?

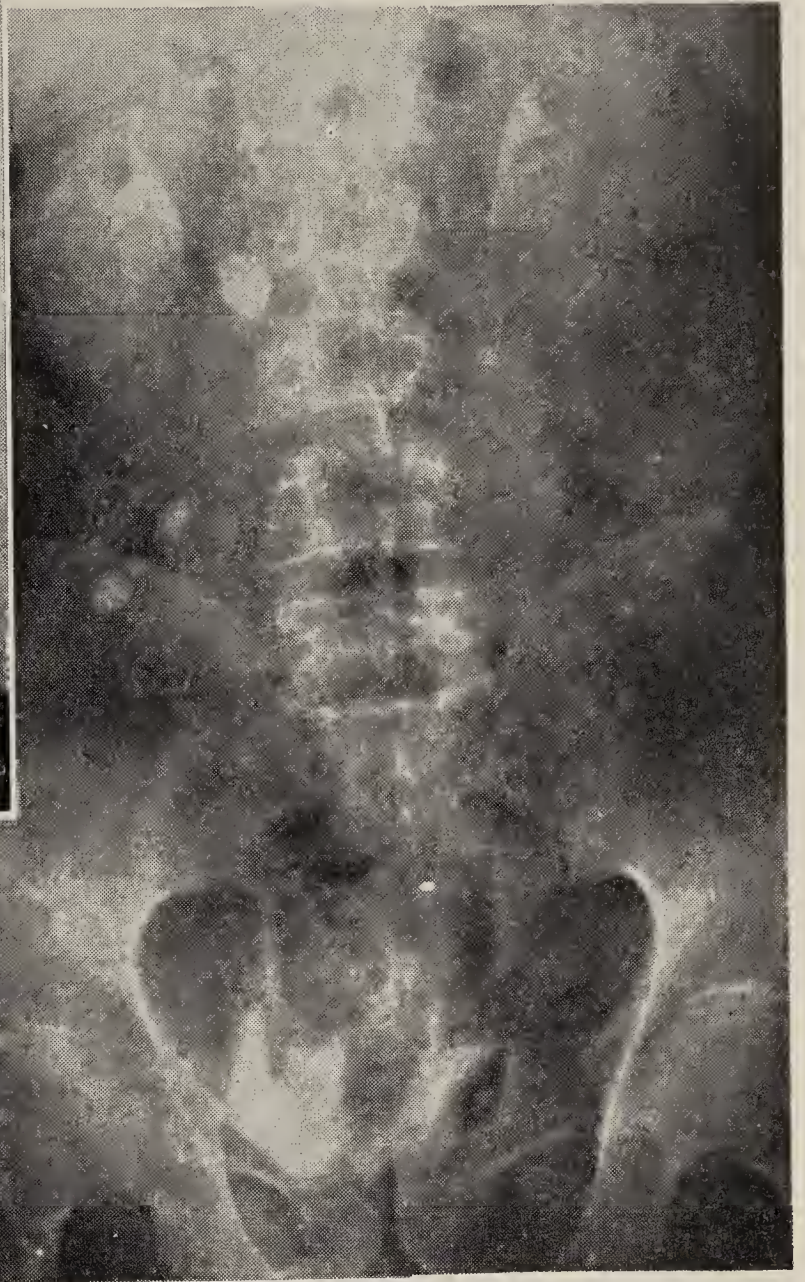
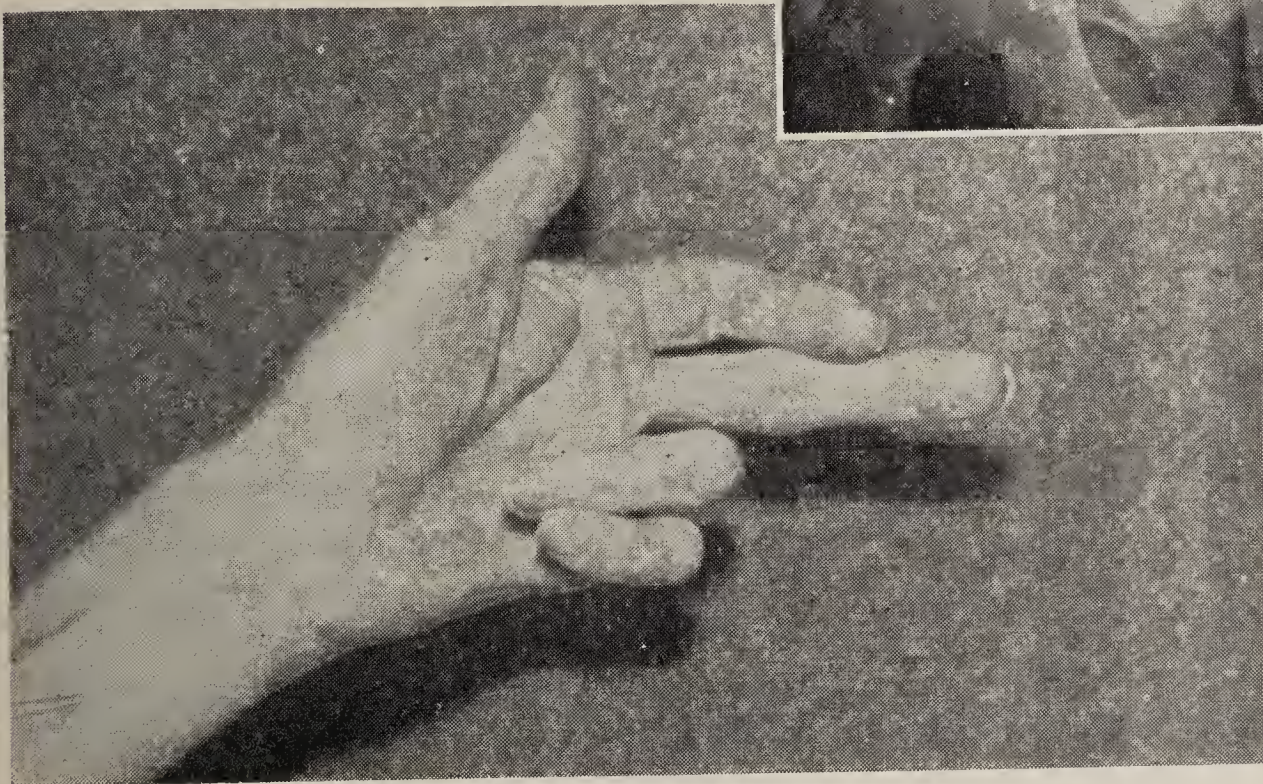


FIGURE 6. There is only one diagnosis here. Can you give the etiology, symptoms, treatment and pathology of this condition?

hormonal imbalance. White has demonstrated that there is an increase in chorionic gonadotrophin and a decrease in estrogen and progesterone during the 23rd to 35th weeks, and states that this abnormality occurs in all diabetic pregnancies which show these complications. Historically this abnormality was first demonstrated in patients suffering from toxemia, and administration of hormones was begun in diabetics only because they were a group known to suffer from a greatly increased incidence of toxemia. Other workers, however, have failed to demonstrate this abnormality in all cases, nor have they been able to show any significant relationship with toxemia. There may also be an abnormality of adrenal corticoids, but the significance of this has never been clearly demonstrated, and in particular its relation to toxemia is not at all well established at present.

Spontaneous premature labour is another complication seen frequently. It is thought by some that Releasin (Relaxin) may be of help in managing this complication.

The major foetal complications are the birth of large oedematous babies, increased incidence of congenital defects, and the great increase in late intrauterine death. The incidence of foetal mortality ranges from 20% to 10% in various series.

Foetal death is related to maternal acidosis, but the mechanism of this death is not fully understood. Recent work by Kaiser and Goodin with normal pregnant women has shown that the foetal pH is slightly lower than the maternal pH, and when the maternal pH is lowered by ammonium chloride, the foetal pH is also lowered. The lowered pH in the foetus is accompanied by an increase in the carbon dioxide content of the blood and an increase in the $p\text{CO}_2$. The lungs and kidneys of the foetus do not function as regulators of the acid-base balance, this function probably being performed

in part by the placenta. There is a time-lag in the decrease of pH in the foetus following decreased maternal pH. It may be that the more rapidly the acidosis occurs, and the longer it lasts, the less able is the foetus to withstand it.

In diabetic acidosis, since the foetus follows the maternal pH due to lack of its own acid-base regulating system, it is not unreasonable to assume that the changed pH of the blood and direct toxic effect of the ketone bodies may cause death of the foetus by interfering with the actively growing tissue and its enzyme systems, or through foetal hypoxia. Foetal death from maternal acidosis does not always occur, but it is the general rule for such to happen. Given reports 41%, Jones 54% and Peel 70% of foetal deaths are associated with episodes of acidosis in the mother. This is very important, for acidosis is preventable.

Prematurity is another cause of infant death. It can be the result of spontaneous premature labour, toxemia, or hydramnios. Some series report that 25% of foetal deaths are associated with toxemia in the mother. Foetal death from such causes will decrease only when these primary maternal complications are decreased.

The last complication, late intrauterine death, has now been nearly eliminated by early delivery. The cause of this death is explained on the basis of the large baby of the diabetic mother receiving inadequate oxygen due to insufficiency of uterine vessels. This is not unreasonable particularly in view of the fact that these deaths occur after the 36th week at a time when the maternal cardiac output is decreasing. In 50% of these late intrauterine deaths, maternal vascular disease is demonstrable (White).

The large oedematous babies seen in diabetic pregnancies are well known. There are several explanations for this: overnutrition due to hyperglycemia and lipemia (but these are not present in the

prediabetic who very often has large babies), oedema (which does not account for the splanchnomegaly), and excessive anterior pituitary activity.

The infant if born alive has other hazards to survive. There is a higher incidence of hyaline membrane disease in the newborn of diabetic mothers; later in life these children tend to be obese; and there is a definitely higher incidence of diabetes in these children than in the population as a whole.

It is beyond the scope of this paper to discuss fully the controversial field of steroid hormone metabolism and steroid replacement therapy in diabetic pregnancies. It suffices to say that Priscilla White and co-workers in Boston state that diabetic pregnancies are characterized by subnormal levels of estrogen and progesterone, and to these they attribute many of the complications of such pregnancies. She gives full replacement therapy with stilboestrol and progesterone to all her patients; she also reports the lowest foetal mortality—10%.

Other workers, however, have not been able to reproduce her results in demonstrating subnormal estrogen and progesterone levels in the diabetic pregnancy or in producing as low foetal mortality *with* the use of hormones. Peel reports 11% foetal mortality in one of his series, Stephens, Holcomb and Page report 8% *without* using hormones. Peel has found a rather consistent lowering of the pregnanediol level preceding intrauterine death, and this may eventually become a practical means of deciding which cases require early delivery.

In conclusion, it is the opinion of this author that hormone replacement therapy is at present not justified in the treatment of pregnant diabetics because the rationale of so doing is not established; it is expensive; it does not prevent the need for early delivery; and it has not been shown that hormone replacement therapy has more to offer the pregnant diabetic

woman and her foetus than does meticulous supervision of the diabetes and conscientious care of the patient by her physician.

The primary requirement in the management of the pregnant diabetic is that the physicians should understand the problem, and be willing to spend a great deal of time and effort in managing the diabetes and the pregnancy. After that, the requirements are *meticulous control of the diabetes and avoidance of ketosis and acidosis, early delivery, and skilled pediatric care for the infant at birth.*

PRENATAL CARE

1. Joint supervision of the pregnancy by an internist and obstetrician who see the patient once every two weeks until the 24th week, and weekly thereafter.

2. Assessment of the patient as to degree of severity of diabetes in terms of White's classification and non-pregnant daily insulin requirements.

3. Diet: 200–250 Gm. carbohydrate, 100 Gm. protein, and the remainder of the caloric requirements made up with fat. Salt intake should be restricted routinely.

4. Patient must be taught to test the urine daily for sugar and ketones.

5. Patient should be checked at visits to the physician for signs and symptoms of diabetes and toxemia. A complete urinalysis, blood sugar, and ophthalmoscopic examination should be done at each visit.

6. Termination for Class F diabetics i.e., those with severe renal and retinal disease.

7. Immediate hospitalization if any of the signs of toxemia, ketosis, acidosis, or infection develop.

8. Routine hospital admission at 32 weeks if financially possible; otherwise, at 34 weeks.

9. Immediate delivery at the danger signals of toxemia, abnormal weight gain, ketosis, hydramnios, or foetal distress

providing the patient has reached 34½–35 weeks. Exceptional circumstances such as poor past history may demand delivery between 32–34 weeks.

The timing of delivery is very important, and requires balancing the risk of late intrauterine death against that of prematurity. The risk of prematurity falls sharply after the 35th week while the risk of intrauterine death increases significantly after the 36th week. Therefore, if at all possible the pregnancy should be continued until the 35th week, and terminated no later than the 36th week. Foetal death often results because delivery has come too soon or too late.

The method of delivery involves a choice between the vaginal route and cesarean section. The advantage of vaginal delivery particularly for the premature child is that it seems to reduce the risk of hyaline membrane disease. The disadvantages are that the weak foetus may succumb during labour, dystocia, and the greater difficulty in controlling the mother's diabetes during labour.

The advantages of cesarean section are the greater ease in controlling the diabetes, the elimination of dystocia, and the avoidance of the trauma of the normal vaginal delivery to the weak foetus. The disadvantages are the increased incidence of hyaline membrane disease and the risk of cesarean section in any person.

Indications for vaginal delivery are termination of pregnancy before 33 weeks, death of the foetus, a multiparous patient with a favourable obstetrical history and favourable cervix, and a primiparous patient with a favourable cervix in good labour. In such patients surgical induction of labour at the 35th week is indicated. Cesarean section is indicated by previous cesarean section, in a primiparous or multiparous patient with an unfavourable cervix, in the presence of

dystocia, and to terminate a spontaneous or induced labour which has not spontaneously terminated after eight hours, or if for any reason delivery is considered urgent.

No sedation should be used in either case except Scopolamine 1/100 mgm. Regional anaesthesia is indicated for vaginal delivery, and epidural or spinal anaesthesia for cesarean section. If labour is induced or cesarean section done electively, then the long-acting insulins should be discontinued the day before and regular insulin substituted. Glucose 10% in distilled water should be given intravenously during the delivery. Forceps are indicated in vaginal delivery.

No hard and fast rules can be laid down regarding the time and method of delivery. The choice varies for each individual patient according to her clinical condition.

Management of the infant at birth is very important. Despite the fact that these infants are large at birth, they are feeble and must be treated as weaklings. In other words they must be given all the care that a premature (which in fact it is) child receives. At birth skilled pediatric care should be immediately available in the delivery room. The infant's bronchial tree and stomach should be aspirated. The child should then be put into a premature incubator, kept in a warm moist atmosphere, given oxygen, and handled as little as possible. Some workers have advocated withholding food for the first 48 hours of life; however, more recently 10% glucose has been given through a gavage tube or per rectum, and this seems to result in a better and earlier diuresis in the infant. Because the mother has received 10% glucose during the delivery, there is little likelihood of hypoglycemia in the infant. After the first 48 hours, artificial feedings are given as indicated by the size and condition of the infant.

The puerperium is usually uneventful, and is characterized by the fact that diabetics do not lactate well.

SUMMARY

Foetal and maternal complications of the diabetic pregnancy have been discussed along with the management of such pregnancies.

ACKNOWLEDGEMENT

The author wishes to thank Dr. R. A. H. Kinch for his very generous help during the preparation of this paper.

BIBLIOGRAPHY

1. EASTMAN, N. J.: *Obs. and Gyn. Survey*, 1: 1, 1946.
2. STEPHENS, BLAIR, HOLCOMB, PAGE: *J.A.M.A.*, 161: No. 3, 224.
3. LONG, HARTMANN, FUTCHER, EASTMAN: *Obs. and Gyn.*, 3: 160, 1954.
4. WHITE, TITUS, JOSLIN, HUNT: *Am. Jour. Med. Science*, 198: 48, 1939.
5. WHITE, P.: *Am. Jour. Med.*, 7: 609, 1949.
6. WHITE, P.: *Surg., Obs. and Gyn.*, 61: 324, 1935.
7. REIS, DECOSTA, ALLWEIS: *Am. Jour. Obs. and Gyn.*, 60: 1023, 1950.
8. TOLSTOI, GIVEN, DOUGLAS: *J.A.M.A.*, 153: 998, 1953.
9. BECK: Textbook.
10. EASTMAN: Textbook.
11. JONES: *Am. Jour. Obs. and Gyn.*, 71: 318, 1956.
12. PEEL: *International Congress of Obs. and Gyn., Geneva*, 1954.
13. PEDERSEN: *Diabetes*, 3: No. 3, 199.
14. DECOSTA: *Obs. and Gyn.*, 5: 401, 1955.
15. KINCH, R. A. H.: *Bulletin, Acad. of Med., Toronto*, 29: 95, 1954.
16. KINCH, R. A. H.: *Personal communication*.
17. GOODIN AND KAISER: *Amer. Jour. Med. Science*, 223: 662, 1957.
18. ROGERS, J. W.: Mimeographed notes.

MULTIPLE PREGNANCY

J. C. C. ALEXANDER, 5T8

FREQUENCY

WITH regard to the frequency of multiple births, it seems that one is not far wrong when he quotes the "rule of 90's" i.e. twins 1:90; triplets 1:90² (8100); and quadruplets 1:90³ (729,000). According to the Metropolitan Life Insurance Company the correct figures are 1:92; 1:9,600 and 1:657,000 respectively.

The relative frequency of multiple births is least among mothers under the age of 20, increases with advance in age to a maximum in their late thirties, and then falls off toward the end of reproductive life.

The likelihood of a multiple birth also depends on the race of the parent. The chances that a negro mother will have twins are 13:1,000 or $\frac{1}{4}$ greater than for white women. The disparity is greater for confinements of more than two babies. Thus triplets are relatively $1\frac{1}{4}$ times as likely among negro mothers as

white, and quadruplets are almost 4 times as likely. The incidence of multiple pregnancy in Mongols is only $\frac{1}{4}$ to $\frac{1}{3}$ that of Caucasians.

Mauriceau in his textbook of 1668 describes the birth of 365 children to Lady Margaret, Countess of Holland, in the year 1313. Such a fantastic figure, although reported in the literature, is difficult to imagine. Several valid births of sextuplets have been reported although none has ever survived. The birth of the Dionne quintuplets in 1934 stimulated interest in multiplicity as no single quintuplet had ever previously survived more than 50 days and no entire set more than 15 days.

AETIOLOGY

To simplify matters, this discussion will deal largely with twins. Twins may be of two types:

1. Double ovum, dizygotic or fraternal

twins resulting from the fertilization of two separate ova expelled from one or both ovaries at the same period of ovulation.

2. Single ovum, monozygotic, identical or homologous twins which are thought to arise in any one of the following ways:

- (a) fission of the blastoderm.
- (b) double gastrulation or the formation of two gastrulae.
- (c) fission of the bilateral halves of a single embryonic axis due to some retarding influence in the development of the ovum.

Heredity is recognized as a factor in the aetiology of multiple birth, and most people believe that it plays its biggest role in fraternal twins. Fraternal twins also increase with advancing parity and age, and are about three to four times as common as the uniovular variety. Similarly triplets and quadruplets may be rarely uniovular or polyovular, but in most cases are a combination of the two types.

Two ova expelled at the same ovulation may be fertilized within a short time of each other. This type of pregnancy is known as superfecundation, and was made famous when a white woman, who, after having had coitus with a white and a black man, gave birth to twins of different colours. Fertilization of two ova derived from different ovulations is termed superfetation.

In dizygotic pregnancies the ova may locate far from each other resulting in two distinct placentae; but if the ova locate close to each other, the placentae may fuse although the circulations are separate. Because each ovum has its own chorion and amnion, where the membranes are apposed, a septum will be found with four layers—an amnion and a chorion from each with occasional remnants of decidua.

The placenta of uniovular twins is

almost invariably single with two cords having anastomoses between them. The septum between ova seldom contains decidua and rarely chorion, and therefore, consists only of two layers from the two amnions. In the rarest cases of uniovular twins, two chorions or separate placentae have been found. The children in these cases are much alike in size, mental and physical characteristics, but fingerprints are not identical. Generally then, if there are two amnions and no chorion in the septum, the twins are uniovular; but if fission occurred in the morula stage of embryonic development, there may be two placentae and two chorions or one placenta and two chorions.

CHARACTERISTICS OF TWINS

(AFTER MACKLIN)

1. If sex the same—identical or fraternal.
If sex opposite—fraternal.
2. If joined or in one sac without septum—identical.
3. If septum—
 - (a) identical if only two amnions.
 - (b) either if two amnions and two chorions, but probably fraternal.
4. If one placenta—identical.
5. If two placentae—either.

FOETAL DEVELOPMENT

Children resulting from multiple pregnancies are generally smaller than those of single births.

In both monozygotic and dizygotic pregnancies one ovum may be expelled, or more commonly may remain in the uterus, and become compressed by the developing ovum thereby becoming known as foetus compressus or papyraceous. If this amorphous mass is retained after birth, it may give rise to postpartum haemorrhage or infection.

Monozygotic abnormalities are usually due to placental anomalies such as unequal distribution and size of placental

vessels resulting in unequal nutritional conditions. Usually the heart of one foetus, being better nourished, is stronger, and the weaker one dilates, the second child becoming a parasite on the first, and known as a foetus acardiacus.

DIAGNOSIS

Multiple pregnancies are accompanied by increased nausea and vomiting, increase in deficiency diseases and increase in preeclampsia and eclampsia. Because of the larger size of the uterus, the pressure symptoms appear earlier with resultant oedema, varicosities of legs and vulva, bladder irritability and dyspnoea. The diagnosis is suspected with increase in size of uterus and multiplicity of small parts on palpation. The positive diagnostic features are:

1. Two heads, two breeches, and one or two backs on palpation.
2. Two hearts with a difference in rate of 10 per minute.
3. X-ray.
4. At delivery of first child.

PRESENTATIONS

The mechanism of adaptation of foetus to uterus is interfered with; therefore, the incidence of malposition and malpresentation is increased. The usual presentations are:

- | | |
|---|----------------------|
| 1. Two heads (usually facing one another)—38% | |
| 2. Head and breech—35% | |
| 3. Two breeches—10% | |
| 4. Head and transverse—9% | } transverse
—15% |
| 5. Breech and transverse—5% | |
| 6. Two transverse—1% | |

MANAGEMENT OF PREGNANCY

The two main complications associated with multiplicity—premature delivery and toxæmia—govern the modification of the usual pregnancy regimes. The patient should avoid strain, and should

therefore, stop work at 24 instead of 34 weeks. She should not travel after 24 weeks because of the chance of premature delivery. She should have long afternoon rests, and coitus should be avoided in the last three months because of the possibility of premature onset of labour. Frequent careful rectal or vaginal examinations should be carried out in the last three months to determine whether the cervix is becoming obliterated and beginning to dilate before the foetuses are viable. If so, labour may be postponed several weeks by confining the patient to bed. The patient should restrict her salt intake when the diagnosis is suspected, and her visits to the doctor should be more frequent than with single pregnancies. Iron therapy should be instituted early, and if the anaemia is refractory to iron, transfusion is indicated.

LABOUR

Overdistension of the uterus is responsible for the infrequent and weak uterine contractions characteristic of multiple pregnancy, and consequently, the first stage is often prolonged. Although the incidence of malpresentation is increased, the incidence of complications does not increase proportionately due to the smallness of the infants. The uterine contractions usually cease after the first child is born. They resume, however, and the second child is quickly expelled, usually within 30 minutes of the first. In 15% of cases the cervix contracts below the presenting part of the second twin, and the first stage must be repeated, further lengthening labour. In the third stage, faulty contractions may produce a delay in separation of the placenta resulting in risk of postpartum haemorrhage. For this reason facilities for transfusion should be available, the patient having been crossed and typed prior to her entering the delivery room.

If the first child presents by vertex or breech, then labour should be managed expectantly. Because of the overdistension, it is often advantageous to rupture the membranes of the first child, thereby aiding the uterine contractions. Prolapse of the cord must, however, be guarded against. In most cases forceps are used unless the mutilation of the patient be great in which instance cesarean section is preferred. Following delivery of the first child, the cord is severed, and uterine contractions awaited. If the membranes of the second child are not ruptured in twenty to thirty minutes, this should be done, and the position of the child checked as it often changes with the birth of the first child. Where a trained anaesthetist is not available, and where the position is longitudinal, voluntary efforts should be encouraged, and pressure on the fundus administered. If delayed by inertia, version and breech extraction should be carried out within 30 minutes.

In most cases of multiple pregnancy in centres with trained anaesthetists, the patient is given deep anaesthesia, and the first baby is extracted by forceps if spontaneous delivery is not imminent. The second child is then delivered with forceps or by podalic version as the case may be. Because of the increased incidence of postpartum haemorrhage, 0.25 mgm. of ergometrine should be administered intravenously with the birth of the second child.

LOCKED TWINS

Locked twins occur 1:90,000 deliveries most often vertex to vertex or breech to vertex, and consist simply of one child jammed against the other so that neither can be expelled. Locked twins may often be displaced by tilting the delivery table and manual palpation especially with locking of two forecoming heads. With locking of the after coming head of the first child and the forecoming head of

the second, often by pushing up and holding the head of the second, the first may be delivered as a breech. If this is impossible, cesarean section, craniotomy, or decapitation may have to be resorted to.

PROGNOSIS

Generally all complications caused by or associated with pregnancy are more frequent in and aggravated by multiplicity. The following figures are after Bender:

	Single	Multiple
Preeclampsia	6.4%	24.0%
Hydramnios	0.5%	10.6%
Accidental Haemorrhage	1.3%	1.7%

The maternal risk is raised due to an increase in toxæmia. Malpresentation often necessitates operative interference with consequent increased chance of infection. As mentioned before, the incidence of postpartum haemorrhage is increased due to the retention of foetal parts or placenta and as a result of the inability of the uterus to contract down in the third stage of labour. The foetal risk is two to three times that of single births because of prematurity, underdevelopment, toxæmia, malpresentation, operative interference and tangling and knotting of cords around each other and around the fetuses.

ACKNOWLEDGEMENT

I would like to thank Dr. John Carmichael, Senior on Obstetrics and Gynecology, Toronto Western Hospital, for his helpful criticism and encouragement in the preparation of this paper.

BIBLIOGRAPHY

1. METROPOLITAN LIFE INS. CO. STATISTICAL BULLETIN: 35, No. 4, 7, 1954.
2. EASTMAN, N. J.: Williams Obstetrics, 11th Edition, 1956.
3. BECK AND ROSENTHAL: Obstetrical Practice, 6th Edition, 1955.
4. GREENHILL-DELEE: Principles and Practice of Obstetrics, 10th Edition.
5. J. CHASSAR MOIR: Munro Kerrs Operative Obstetrics, 6th Edition.
6. BENDER: *Jour. Obs. and Gyn.*, 59: 510, 1952.

VAGINAL BLEEDING* : Part I

P. G. WALFISH, 5T8

INTRODUCTION

THE purpose of this paper will be:

1. To outline the scope of such a topic.
2. To suggest a mode of classifying clinically the many causes.
3. To present theories of the mechanism of bleeding for the causes discussed (if a theory exists).
4. To give a brief description of the main clinical features and the essential investigations which will aid in the differential diagnosis.

The topic of vaginal bleeding can be said to include any clinical condition, both physiological and pathological, occurring at any age from infancy to senility, in which the symptom or sign of blood, whether it be alone or mixed with other substances, is found in the vagina.

When attempting to classify the possible etiology of vaginal bleeding, one must first decide whether the source of the bleeding is uterine or extra-uterine. If it is uterine in origin, is the bleeding pathological or physiological? When thinking in terms of etiology, it would be helpful to be able to classify all causes in relation to the most common yet physiological cause of vaginal bleeding, namely, the cyclic bleeding of menstruation. Vaginal bleeding could then be considered according to whether it occurred during, before, or after that stage of life when the cyclic bleeding of menstruation occurs. If it is during this stage, the presence or absence of pregnancy must be established. If pregnancy is present,

*ED. NOTE: Because of the scope of this topic, it will be presented in two parts, the first dealing with bleeding in the absence of pregnancy, and the second, to be published in a subsequent issue, dealing with bleeding associated with pregnancy.

it must be decided whether the cause of bleeding is related to the pregnancy or merely an unrelated complication.

This Part will deal in greater detail with the numerous subdivisions which can be assigned to the basic aforementioned factors in classifying and establishing the causes of vaginal bleeding *not* related to pregnancy.

UTERINE BLEEDING

I. DURING PHASE OF CYCLIC BLEEDING OF MENSES (REPRODUCTIVE ERA)

A. NORMAL CAUSES:

1. Menstruation
2. Ovulation

These causes of uterine bleeding are related to the normal endocrine dynamics of the female. While the cyclic bleeding occurring with menstruation is universal, the bleeding associated with ovulation is very uncommon and not well explained, being related either to a temporary lowering of the estrogen level or to rupture and bleeding into the early corpus luteum.

CLINICAL FEATURES OF MENSTRUATION

Definition: A lochial discharge following abortion of a non-fertilized ovum resulting in a periodic sanguinous discharge from the endometrium recurring at approximately monthly intervals from the time of puberty until the menopause, being absent normally during pregnancy and lactation.

Duration: An average menstrual cycle takes 28 days but this actually occurs in only 15% of women. The remainder range from 21-31 days. The duration of the menstrual flow varies from 3 to 5 days. "Regardless of the different frequencies, the length of each woman's cycle is

within a few days of the average length of all her cycles."¹

Age of onset: Most commonly in this country from 11–16 years.

Age of cessation: Commonly age 45 to 50 with a possible range of 35–55, the usual rule being the later the onset, the earlier the cessation.

Characteristics of discharge: It is composed of altered blood, uterine secretions, mucus and tissue detritus from the desquamating endometrium together with obscure substances which can cause vasoconstriction or fibrinolysis. Menstrual blood does not coagulate; this is believed to occur because of its passage through the endometrium with resultant loss of prothrombin and fibrinogen due to fibrinolytic enzymes present in the premenstrual and menstrual endometrium. Blood from the cervix, however, retains its ability to coagulate. The amount of discharge considered within normal range varies up to several ounces, the average loss being 1 oz. Bleeding is most profuse during the early part of menstruation.

B. ABNORMAL CAUSES:

Causes of uterine bleeding occurring when the menses are functioning will reveal themselves clinically by a deviation from the normal pattern of cyclic bleeding in one way or another i.e. in frequency, duration, amount, or combinations of these.

The causes of abnormal uterine bleeding in the absence of pregnancy may be classified as follows:

1. Functional or endocrinopathic aberration of menses.
2. Local pathological lesions within the generative organs.
3. Other systemic and constitutional influences.
4. Combinations of the above.

I. FUNCTIONAL OR ENDOCRINOPATHIC ABERRATION OF MENSES

The common definition is "bleeding

that is not associated with neoplastic, inflammatory or trophoblastic change within the pelvis."⁸ Yet, not infrequently common pathological changes such as leiomyomata are found associated with a functional disorder, and it is not known whether this is a cause or an effect of the endocrine disturbances, or just an unrelated lesion.

This condition may occur at any time during the reproductive stage and occasionally outside the reproductive era. Greater than 50% of the cases are encountered in preclimacteric life—roughly the 5th decade; 15% of the cases are found at or near the age of puberty. The remaining 30–35% are distributed uniformly throughout the intervening years of menstrual life.²

Bleeding may be menorrhagic, metrorrhagic or a combination of the two, but the periodic type is more characteristic. The amount of bleeding varies from moderately excess to profuse. Menstrual rhythm may be normally maintained, quickened or retarded. Non-bleeding phases of considerable duration can be interposed between periods of profuse bleeding, and this is especially true in pre-climacteric and pubertal cases.

Not all cases of functional bleeding show a similar histological picture. This seems to indicate that there are several different causes and mechanisms involved. It is known that there is frequently a disparity between the growth and bleeding effects of estrogenic hormone upon the endometrium. The endometrium may be completely normal, atrophic, hyperplastic, or show only slight growth effect. It is likely that certain endometria are refractory to the growth effects of estrogen, yet are sensitive to the periodic falls of estrogen levels, thereby resulting in episodes of uterine bleeding. It is also known that the menstrual cycle may continue without ovulation in which case the endometrium regenerates and proliferates,

but does not show evidence of secretory activity. The cycle is then called anovulatory in contra-distinction to the normal ovulatory cycle. The clinical types of functional bleeding are:

a. OVULATORY FUNCTIONAL BLEEDING

Histology: Endometrial biopsy reveals secretory or menstruating phase.

Theoretical Mechanism: A quantitative imbalance between the two ovarian hormones, progesterone and estrogen, but other postulated factors are an extra-ovarian bleeding factor of as yet unknown origin, dysfunction of uterine musculature or vasomotor nerves, and disorder of the spiral arteriolar system.

b. ANOVULATORY FUNCTIONAL BLEEDING

Perhaps the largest number of cases of functional uterine bleeding are found related to a feature of ovulation. This occurs most frequently soon after puberty and near the menopause while in young adults less than 5% of cycles are anovulatory.

Histology: Endometrial biopsy before expected bleeding shows either a proliferative endometrium or an exaggeration of the proliferative phase called endometrial hyperplasia, with polypoid thickening, patchy necrosis of the superficial layers and cystic dilatation of the glands giving a "swiss cheese" appearance, but no secretory endometrium.

Theoretical Mechanism: Hypofunction of the anterior pituitary will result in failure of ovulation. Since no corpus luteum is formed, progesterone is not produced, and therefore the endometrium does not progress to a secretory phase. Imbalance of estrogen and progesterone levels with a relative excess of estrogen results in stimulating the endometrial spiral arterioles with consequent bleeding and shedding of the endometrium. However, when a series of such follicles develop but do

not rupture, as described by Shroeder as "metropathia hemorrhagica", resulting in cystic ovaries, absent corpora lutea and progesterone, or when there is a continuous low grade estrogen stimulation from any other source but not sufficient to produce a luteal secretory phase e.g. estrogen producing ovarian tumors, overtreatment with estrogen hormone or Vitamin B complex deficiency (which impairs the ability of the liver to destroy circulating estrogens), then an exaggeration of the proliferative endometrium results in hyperlasia. This type tends to bleed profusely with any fall in estrogen level, but the onset of bleeding is often preceded by several weeks of amenorrhea.

c. DELAYED OR IRREGULAR SHEDDING OF ENDOMETRIUM

This is a relatively uncommon cause of bleeding, and one which is easily overlooked.

Histology: Degenerated endometrial glands within retained hyalinized tissue together with islands and rests of definitely secretory endometrium are still present toward the end of the bleeding phase.⁸

Theoretical Mechanism: It is possible that this hyalinized tissue retained through the bleeding phase of menstruation may continue as a stimulant for further bleeding. This leads to prolongation of the desquamation phase of menstruation, thereby prolonging the menstrual flow.⁸

2. LOCAL PATHOLOGY OF THE GENERATIVE ORGANS

This includes lesions which involve the ovaries, fallopian tubes, uterus and cervix. Many of these lesions may possibly have an endocrinological basis related to ovarian dysfunction and/or the endometrium. It has been said that "as a

rule, any instance of (uterine) bleeding that is associated with pain or leukorrhea is traceable to some local organic cause."⁵ Careful distinction between the nature of menstrual flow, mainly pure menorrhagia from metrorrhagia serves to distinguish many of the conditions found in this category.

(1) MENORRHAGIA—CLINICAL FEATURES OF LESIONS

a. BENIGN GROWTHS

(i) *Fibromyomata*: Simple bimanual examination reveals a tumor usually asymmetrical; and if there is more than one tumor, the uterus is enlarged, irregular in shape, and usually hard and unyielding in consistency unless cystic degeneration develops thereby giving a fluid thrill. The tumor and the cervix move together if the organ can be moved at all. Differentiation of a fibromyoma from an ovarian cyst may be difficult, but the latter rarely gives rise to any menstrual disturbance unless amenorrhea. Usually the diagnosis is clear after simple examination, but if it is not, a uterine sound can be passed if there is no possibility of pregnancy. Commonly it will pass more than 2½ inches and may go as far as 6 inches when a fibromyoma is present while with ovarian cysts the length of the uterus is not increased.⁴

(ii) *Adenomyosis and Endometriosis*: There is a moderately and diffusely enlarged uterus firmly fixed to the pelvis with one or more small nodules palpable in the region of the utero-sacral ligaments. When this is combined with menorrhagia in the latter part of reproductivity and a colicky dysmenorrhea referred to the rectum, lower sacrum or coccygeal regions, there is little doubt as to the presence of endometriosis probably combined with adenomyo-

sis. In many cases, pelvic endometriosis does not co-exist, and the diagnosis although strongly presumptive cannot be made until post-operative pathological studies are done.

b. INFLAMMATION

(i) *Acute Endometritis*: This may occur as a post abortal or post partum complication. A chronic menorrhagia occasionally develops.

(ii) *Chronic Endometritis*: Most of these patients have had pregnancies, but endometritis may occur in a virgin as a result of infection. This condition cannot be proven without curettage of the endometrium and microscopic examination of the curettings to show a leukocytic infiltration and the presence of plasma cells in a stroma of thickened mucous membrane with flattened or tall columnar epithelium (glandular hyperplasia).

(iii) *Salpingo-oophoritis or Adnexitis*: Inflammation of the fallopian tubes and ovaries may not only cause menstrual bleeding but also disturbances of menstrual rhythm in the form of shortened intervals. In many cases, however, the immediate factor is likely ovarian dysfunction rather than pelvic hyperemia.

c. UTERINE DISPLACEMENTS

(i) *Retroversion and Flexion of the Uterus*: This may be congenital or acquired in nature. Backache is frequently present, but menstrual disorders do not necessarily occur. Menorrhagia, when present, is accompanied by dysmenorrhea, and usually occurs in the acquired type where extreme inflammatory disease and leukorrhea may be found.

(ii) *Subinvolution of the Uterus*: This is seen most often with marked flexion and retroversion of the uterus due to incompleteness of the nor-

mal involution of the puerperium leaving a large, boggy, and congested uterus.

(2) METRORRHAGIA—CLINICAL FEATURES OF LESIONS

“With the exception of obvious mucous polypi, fibroid polypi and advanced neoplasms of the cervix, all growths of the uterus require a preliminary histological examination for their exact diagnosis unless symptoms demand a radical operation and the nature of the growth can be determined after removal.”

Mucous polypi and fibroid polypi are common causes of intermenstrual bleeding. These are quite definite and obvious in appearance. Mucous polypi are soft, strawberry red in color, pedunculated and contain cystic spaces filled with a glairy mucus. They may attain a great size. Fibroid polypi are hard showing the typical glistening whorled appearance on cross-section. Fibromyomata, it has been said, give rise to pure menorrhagia except when they are submucous in origin and in the process of extrusion become polypoid. Polypi become liable to infection and sloughing in their dependent portions due to interference with their blood supply by pressure of the cervical canal or cervix. This also gives them the tendency to bleed more or less constantly. Cervical mucous polyps give rise characteristically to slight intermenstrual bleeding provoked by muscular exertion or coitus, being very similar clinically to early stages of cervical carcinoma; whereas endometrial polyps, due to their protected position in the uterine cavity, rarely bleed unless they become large and prolapse into the cervical or even vaginal canal when they are accompanied by ulceration.

The differential diagnosis of carcinoma, erosion or tubercle of the cervix is often difficult in the early stages. The bleeding in cancer is the result of surface ulceration present even in the early stages of

malignancy. If the cancer is advanced, the friable nature of the growth which can be broken down with the finger distinguishes it at once from the leathery hardness of the normal cervix and the removable velvety surface present in erosions. Similarly tubercle of the cervix can be confusing, and in the early stages only a biopsy and microscopic studies of the cervical region will enable a distinction to be made.

Adenocarcinoma of the corpus uteri gives uterine bleeding during the reproductive era in only about 25% of cases, the remainder being post-menopausal. It is especially significant when it is intermenstrual, but in the early stages it may appear as only a slight blood-tinged watery discharge. There is rarely much increase in uterine size. Leukorrhea is more common in carcinoma of the cervix due to the increased opportunity for infection.

Sarcoma arises *de novo* in the cervix, ovary, or uterus, or as a sarcomatous degeneration of fibromyomata (0.5%). It is far less common than carcinoma but produces bleeding of the same type. Rapid enlargement of the uterus or cervix with irregular hemorrhage is very suggestive of sarcoma, but it is not uncommon for several fibroids present in the same uterus to undergo rapid enlargement because of degenerative changes while hemorrhage occurs due to the extrusion of another.

Chorionepithelioma, a tumor of foetal trophoblastic origin, is exceedingly rare. It is to be suspected when there is persistent bleeding after the evacuation of a hydatidiform mole (which is the source in 50% of the cases although not more than 1–2% of benign moles undergo malignant change), after a miscarriage or often after a full term delivery. Profuse bleeding and rapid development of a foetid discharge due to the decomposition of blood and necrotic tissue *in utero* which is more

foul than with carcinoma of the uterus are usually present. Repeated quantitative studies of choriogonadotrophin in urine will aid in the diagnosis. Usually the diagnosis is not made until the later stages when metastases begin to appear in the vagina, vulva and lungs as dark hemorrhagic nodules. "The decisive diagnosis of chorionepithelioma must be made by microscope and not by hormone studies."⁴

Where abdominal pain precedes slight metrorrhagia, one must consider rupture and hemorrhage into a maturing follicle or early corpus luteum, torsion of ovarian cyst and falls or blows on the abdomen.

3. OTHER SYSTEMIC AND CONSTITUTIONAL INFLUENCES

These are the least common causes but nevertheless must be considered.

a. *Acute infectious diseases*: Typhoid fever, pneumonia, influenza, cholera, scarlatina, malaria, diphtheria, measles and variola all may cause transient bleeding, menorrhagic in type, although amenorrhea is more common.

b. *Chronic infection*: Tuberculosis, even if completely extragenital, can cause bleeding as a result of increased blood vessel permeability due to constitutional depravity. In chronic nephritis bleeding may be due to hypertension.

c. *Circulatory system*:

(i) Hyperemia of pelvic organs with a resultant menorrhagic type of bleeding may be due to increased back pressure of the venous system as in uncompensated valvular heart disease, cirrhosis, or emphysema; or to increased circulation as in hypertension.

(ii) Changes in the blood itself: Hypoprothrombinemia and vitamin K deficiency, purpura, scurvy, deficiency of calcium salts near the menopause, anemia and leukemia.

(iii) High blood pressure: This must be reckoned as a cause of menorrhagia at any period of life, but particularly when nearing the onset of the menopause. Arteriosclerosis and essential hypertension are considered to be the underlying causes. Yet some cases may eventually prove to be related to the internal secretion of the ductless glands, for many women have raised blood pressure at the time of menopause which becomes normal spontaneously a year or two later.

d. *Chronic Intoxication*: Phosphorus, lead, alcohol.

e. *Nervous system*: The exact role the nervous system plays is obscure. However, it is never the cause of a lasting menorrhagia, but may be responsible for a single profuse period related to:

(i) A temporary disturbance of the autonomic nervous system e.g. fright, shock or excessive physical exertion.

(ii) Coitus and reflex uterine congestion e.g. coitus interruptus, prevention of contraception, sexual excess—especially in the early months of marriage.

"In any case one is not justified in assuming that the nervous system is at fault in menorrhagia until by careful investigation one has eliminated all important causes."⁴

II. ABNORMAL UTERINE BLEEDING—MENSES NOT FUNCTIONING

This will occur in but three situations: (1) before puberty, (2) post menopausal, (3) pregnancy and lactation.

1. BEFORE PUBERTY

a. *Functional or Endocrinopathic*

(i) Uterine bleeding of the newborn may occur as a result of uterine congestion subsequent to the cessation of the placental circulation resulting in a temporary high concen-

tration of estrogen suddenly being reduced. The bleeding is usually trivial.

(ii) Pubertas Praecox: This is a premature production of a normal physiological process occurring from 6–12 years of age due to a premature awakening of the pituitary-gonadal axis. Sometimes hypothalamic disease is responsible.

(iii) Pseudo Pubertas Praecox: This is a false maturity associated with pathological lesions such as estrogen producing tumor of ovary or adrenal.

(iv) Anovulatory bleeding i.e. prior to the onset of the regular menstrual cycle.

b. *Local Pathological Lesions*

The main unusual and most fatal lesion is sarcoma of the cervix.

2. POST MENOPAUSAL

a. *Functional*—as described in anovulatory functional bleeding.

b. *Local Pathological Lesions*

(1) Neoplasms

(i) Malignant growths must always be suspected and therefore microscopic studies of biopsies or D & C must never be omitted—carcinoma of body of uterus, carcinoma of cervix, sarcoma, estrogen producing ovarian tumors—theca and granulosa cell.

(ii) Benign growths—mucous polypi, fibromyomata, adenomyosis, endometriosis.

(2) Inflammation

(i) Chronic or Senile Endometritis.

(ii) Pyometra: Distension of the uterus with pus giving rise to hemorrhage with a foul discharge is almost always due to a malignant growth but sometimes only an infection.

EXTRA-UTERINE BLEEDING

The symptom or sign of blood in the

vaginal region due to extra-uterine sources occurs mainly from the vagina, vulva and urethra. Other sources such as the perineum and the rectum must be mentioned, but only because the patient may confuse these sources with vaginal bleeding.

These extra-uterine sources and their lesions may be classified as follows:

1. TRAUMA

Traumatic injury to the vulva, vagina, and urethra most commonly results from mechanical injury—as a result of precipitous childbirth and operative interference at delivery, attempts to produce abortion, and following coitus or abnormal sexual practices. Chemical injury is most frequently seen after an attempt to produce abortion by the insertion of potassium permanganate tablets into the vagina, thereby producing a profuse hemorrhage.

2. INFLAMMATION

Senile or atrophic vaginitis gives rise to bleeding which is slight, intermittent and bright red in colour, accompanied by itching, burning and soreness of the vagina. Speculum examination reveals inflamed fornices and granulation tissue which may bleed if the surfaces are rubbed together. The surfaces may be adherent but separable. Attempts to separate the surfaces may cause bleeding. These clinical features are a result of atrophy of the vaginal mucosa which normally occurs at the time of the menopause, thereby becoming less resistant to minimal trauma or infection.

The mucous membrane of the vagina is also susceptible to the diseases of mucous membranes elsewhere. Such diseases as erythema nodosum or bullous cause pyrexia and mucous membranes which have crusts and bleed easily with the slightest touch. The skin is almost always involved if the mucous membranes are.

Leukoplakia of the vulva shows in its

early stages a redness of the affected skin, which is usually locally or diffusely situated on the labia. It is also whitish and parchment-like, cracking easily with fissures that bleed slightly and itch intolerably. This lesion is believed to strongly predispose to cancer.

3. CIRCULATORY DISORDER

Varices especially in the labia are usually seen in women suffering from either varicose veins in the lower pelvis or increased intra-pelvic pressure due to pregnancy or large tumors. These swell with blood on standing and disappear on reclining. "Rupture of varices in the vagina and the vulva is uncommon apart from child-birth, but occasionally follows injury. When rupture occurs profuse bleeding often follows."³

4. NEOPLASMS

a. *Benign*

These are extremely rare causes of vaginal bleeding. Urethral caruncle is a clinical rather than a pathological term which refers to a small growth from either the meatus or from the urethra just within the meatus. It is only the vascular variety of this growth that is associated with bleeding precipitated by slight trauma or activity.

Hidradenoma of the vulva is a rare lesion appearing on the labia majora or minora or perineum. The overlying skin is reddened, granular, ulcerated and bleeding. Since it is often mistaken for adenocarcinoma microscopically, it must be considered.

b. *Malignant*

Bleeding occurs only when ulceration is present.

(i) Primary

Carcinoma is almost always the

epidermoid variety, and may occur in the vulva or vagina, being more common in the former where in 50% of cases it is preceded by leukoplakia. Sarcoma is rare but may occur at any age, and the grape-like variety of sarcoma, botryoides, of infancy or early childhood in the cervix or vaginal vault is highly malignant.

Melanoma is a primary tumor of the vulva and is very rare.

(ii) Secondary

Tumor metastases in the vulva are found in the late stages of adjacent diseased pelvic structures, such as cervix and corpus uteri, and rarely, in the very late stages of malignancy in distant organs.

ACKNOWLEDGEMENT

The author wishes to thank Dr. W. H. Allemang for his helpful criticism in the preparation of this paper, and Mrs. T. Carey for her invaluable assistance in typing the manuscript.

BIBLIOGRAPHY

1. BECK, A. C., AND ROSENTHAL, A. H.: *Obstetrical Practice*. Sixth Edition, 1955.
2. NOVAK, E. M., AND NOVAK, E. R.: *Textbook of Gynecology*, Fifth Edition, 1956.
3. SCOTT, W. A., AND VANWYCK, H. B.: *The Essentials of Obstetrics and Gynecology*, 1948.
4. DOUTHWAITE, A. H., Editor: *French's Index of Differential Diagnosis*, Seventh Edition, 1954.
5. MERCK MANUAL: Ninth Edition, 1957.
6. RATNOFF, O. P., PRICHARD, J. A., CALAPY, J. E.: *New Eng. Med. Jour.*, 63: No. 97, 253, 1955.
7. McLENNAN, C. D.: *Am. Jour. Obs. and Gyn.*, 68: 315, 1954.
8. MOORE, J. G., SINGH, B. P., HOLZMAN, R. S.: *Univ. of California Med. Jour.*, 81: 316, 1954.

ANSWERS TO "ON INSPECTION"

B. M. STEWART, 5T8; R. C. BULL, 5T8

FIGURE 1. This slightly raised, flat lesion on the lower lip, with a shallow central ulceration can only be a primary squamous cell carcinoma. It is mainly a disease of males, and 95% are said to be on the lower lip. Much emphasis has been placed upon chronic irritation such as sunlight and weather as a cause of lip cancer. Actually this man was a farmer. Some pathologists blame pipe smoking, but from the even line of this man's teeth where he would hold the pipe stem, it is evident that smoking is not a factor here.

The disease is more common after the age of 40.

Squamous cell carcinoma of the lip metastasizes very slowly. Two methods of treatment are available: surgery and radiation. Surgery consists of a V-shaped incision widely skirting the lesion. Skin flaps from the cheek may be necessary. Radium needles produce good results. The needles should extend 0.5 cm. beyond the visible edge of the tumor.

Ref.: IAN AIRD: Companion in Surgical Studies, 2nd Ed., 1957.

FIGURE 2. These lesions are the result of treatment by the age old custom of cupping. The patient's doctor was probably European, for North American medical schools abandoned this practice over thirty years ago.

Blood was removed in certain sicknesses because it was considered to be poisoned. The physician heated a wide mouthed flask, thereby expanding the contained air, and then applied its mouth to the patient's skin. As the air cooled, it contracted, creating enough suction to draw several cubic centimetres of blood from the skin capillaries.

The pathology is merely epidermal

hemorrhage.

Ref.: WARDROP, J.: A Treatise on the Curative Effects of Bloodletting, 1837.

FIGURE 3. The texture of the skin and the smooth contours suggest that this woman is of child bearing age. Thus, the differential diagnosis can be limited to unilateral breast lesions involving the whole breast in a woman of this age group.

The common lesions include acute mastitis, chronic mastitis, fat necrosis following trauma, single cyst, multiple cystic disease, and carcinoma.

This photograph was chosen because of the retraction of the nipple and the appearance of tumour above it suggesting mammary carcinoma. The actual diagnosis is acute mastitis. Nipple retraction can be misleading!

FIGURE 4. This is obviously a pseudo-hermaphrodite, but the dehydration of surrounding tissues should suggest the adrenal origin i.e. congenital virilism due to a genetic failure to synthesize glucocorticoids. These children may exhibit Addisonian crises in the absence of stress or infection.

The treatment is Cortisone 25 mgm. daily. Cortisone inhibits ACTH production, and thereby prevents abnormal steroid production by the adrenal cortices which become atrophic.

The basic defect lies in a deficiency of the enzyme 17-hydroxylase resulting in impairment of cortisone synthesis and promotion of pituitary over compensation via excess ACTH secretion. The ACTH causes excess adrenal androgen formation and hence, the virilism. The administration of Cortisone depresses ACTH production, and indirectly inhibits androgen synthesis.

A dwarf with amastia and amenorrhea will result if treatment is not instituted before puberty.

Ref.: SAMSON AND WILKINS: *Jour. of Ped.*, 1956.

FIGURE 5. A description of this X-ray should include mention of:

- a. the lumbar scoliosis.
- b. the complete fracture of the left pubic bone with displacement of the superior ramus.
- c. extravasation of introduced dye beyond the normal limits of the bladder i.e. ruptured bladder.
- d. good visualization of both ureters and renal pelves with normal configuration.
- e. three calcified lymph nodes along the right common iliac artery and one calcified para-aortic lymph node.

This 48-year-old alcoholic was bull fighting automobiles with his coat while drunk when he was struck by one of them, fracturing his left femur and pelvis, and rupturing the bladder.

It is obvious that this man came to hospital due to his injuries sustained through trauma. He would suffer from severe lower abdominal pain and anuria.

FIGURE 6. This is a classical example of Dupytren's Contracture or Palmar Fascia Contracture.

The palmaris longus muscle inserts into the palmar fascia. Hypertrophy of the muscle begins with nodular thickening of the fascia overlying the flexor tendons to the ring finger. With progression the other fingers are successively involved. Contraction proceeds gradually, and is first manifested as skin dimples.

Dupytren's Contracture often occurs bilaterally, and may be hereditary. It is also seen in the feet and in the penis (Peyronie's Disease).

Very little is known of its etiology. Trauma is not important, many cases being seen in clerical and professional workers.

The condition is usually symptomless. Sometimes pain is apparent at the nodules.

Treatment consists of excision of the palmar fascia, and movement usually returns well without physiotherapy.

Ref.: 1. FERGUSON, L. K.: *Surgery of the Ambulatory Patient*, 3rd Ed.

2. KANAVAL, SUMNER *et al.*: *Surg., Obs., and Gyn.*, 48: 145-190, 1929.

ACKNOWLEDGEMENT

The editors are grateful to Dr. A. L. Chute, Dr. R. A. Mustard, Dr. A. S. Mallam, Mr. L. Solursh, Mr. F. Athran, and Mr. A. Smialowski for their permission in making these photographs available to the Journal.

BOOK REVIEWS

BASIC NUTRITION. E. W. McHenry, Professor of Public Health Nutrition, School of Hygiene, University of Toronto. 380 pp. J. B. Lippincott Company, Montreal, 1957.

This text has been written to present nutrition at the university level.

The script is well organized, and reads easily. Understanding of the material

presented depends on the reader's knowledge of the basic physical, chemical, biological and medical sciences; hence, it is ideally suited to the senior medical student.

The author covers energy requirements; the basic foods carbohydrate, protein, and fat; the nutritional elements; and the preventive aspects of malnutri-

tion. The sections dealing with vitamins and special diets are especially noteworthy.

The entire book is written with clarity and authority. It will be a valuable addition to the student's library on a subject which is diffusely presented throughout medical school.

HISTOLOGY. Arthur Worth Ham, Faculties of Medicine and Dentistry, University of Toronto. 874 pp. Illust. 3rd ed. J. B. Lippincott Company, Montreal.

The major reason for the writing of the 3rd edition of this universally respected text is the dramatic development of electron microscopy over the past four years. The chapter on the mechanism and use of the E/M has been considerably expanded.

In order to add some sixty new figures and colour plates to the text along with

the massive amount of new histologic information exposed by the electron microscope while maintaining the previously established scope of subjects covered, virtually the entire book has been rewritten. That this has been extremely well done is witnessed by the fact that the 3rd edition is only thirty pages longer than its predecessor.

The now well-known style of integrating histology with the other basic sciences of anatomy, physiology, pathology, and biochemistry has been preserved.

Chapters receiving more extensive revision are those dealing with transplantation of tissue, blood clotting, cell differentiation and tissue culture, bone, hemopoietic tissue, and teeth.

This new edition, completely up-to-date, must take its place among the textbooks of choice.

A. C. S.

NEWS AND NOTES

DR. R. M. JANES, recently retired as Professor and Head of the Department of Surgery, has been appointed a Sims Commonwealth Travelling Professor of Surgery for 1958 by the Royal College of Surgeons, England. Dr. Janes will visit medical schools and universities in Jamaica, West Africa, South Africa and East Africa.

PROFESSOR F. G. KERGIN has been appointed Head of the Department of Surgery and Surgeon-in-Chief at the Toronto General Hospital.

DR. TREVOR OWEN has retired from active teaching in the Department of

Medicine. His great service as a teacher over many years will be missed.

MR. SAUL SIDLOFSKY of Meds 5T8 represented this school at the Clinical Congress of the American College of Surgeons, October 14-18, in Atlantic City.

DR. J. V. BASMAJIAN has left the Department of Anatomy to take up new duties as Professor and Head of the Department at Queen's University.

A DISTINGUISHED VISITOR here on an exchange programme for the month of October was Dr. Evan Bedford from Middlesex Hospital, England.

FURTHER PRODUCTION EXPANSION COW & GATE (CANADA) LIMITED

The steadily growing demand for FARMER'S WIFE from all parts of Canada has necessitated a further substantial increase in production facilities to assure that fresh supplies of these specially prepared infant feeding formula milks may remain constantly available for all areas.

To service the requirements of users in the Maritime Provinces a special arrangement has been made with Central Creameries Limited at Charlottetown, P.E.I. to produce FARMER'S WIFE in their newly established Evaporated Milk Plant, using the exclusive Cow & Gate process under the supervision of our own technicians.

The expanding requirements of our customers in Quebec, Ontario and Manitoba will continue to be supplied entirely from our modern plant in Brockville, Ontario, as at present.

FARMER'S WIFE

COW & GATE (CANADA) LIMITED

"Specialists in the Processing of Milk Foods for Infant Feeding"

During Pregnancy and Lactation



"FERROGEN" BRAND COMPOUND

Ferrous sulphate B P 325 mg. (5 gr.)
*Bone flour (edible).... 325 mg. (5 gr.)
Vitamin A (acetate)..... 1500 I.U.
Vitamin D 500 I.U.
Vitamin B₁ 1 mg.
Riboflavin 1 mg.
Niacinamide 5 mg.
Vitamin C 30 mg.
Sodium iodide... 0.2 mg. (1/300 gr.)

*Average content: calcium 110 mg., phosphorus 50 mg., fluorine 0.4 mg., and other trace elements.

Bottles of 100 tablets.

IRON
CALCIUM
IODINE
MINERAL
AND
VITAMIN
TABLET

DOSAGE: In order to establish tolerance to iron, full dosage should be arrived at gradually. One tablet daily after the main meal for several days, increased to two tablets daily, one after breakfast and one after lunch for several days and, finally, one tablet three times daily after meals.



Charles E. Frosst & Co.
MONTREAL CANADA

Now available in **Canada**
 a new soluble single sulfonamide



solusulfa

SULFAETHYLTHIODIAZOLE

-  reaches therapeutic blood levels rapidly
-  remains up to eight hours
-  almost exclusively in the plasma
-  in it's active "free" form

Solusulfa Tablets—100's Solusulfa Liquid—8 oz.
 0.5 grams sulfaethylthiodiazole per tablet or teaspoonful.

FRANK W. HORNER LIMITED • MONTREAL, CANADA



routine

in the six-week postpartum checkup

- A** GENERAL PHYSICAL, including blood and urine
- B** THOROUGH PELVIC EXAMINATION
- C** COUNSEL ON FUTURE PREGNANCIES



THE SPERMICIDAL GEL WITH BUILT-IN BARRIER



*Trade Mark Reg'd.

PUBLISHED

JUST

CIBA COLLECTION OF MEDICAL ILLUSTRATIONS

LIVER, BILIARY TRACT AND PANCREAS

Part III of Volume 3: Digestive System*

Illustrated by Frank H. Netter, M.D.,
Edited by Ernest Oppenheimer, M.D.,
assisted by 5 outstanding teacher-physicians.

Sold at cost \$10.50

*Parts I and II available at a later date.
Also available: Nervous System, Reproductive System,
The Hypothalamus.

C I B A 1235 McGill College Ave., Montreal 2, P.Q.